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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,779	07/13/2001	Venkatraman Ramakrishnan	256602000500	1824

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EXAMINER	
LY, CHEYNE D	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/904,779	RAMAKRISHNAN ET AL.	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *5-11* is/are withdrawn from consideration.

5)☒ Claim(s) *1, 2, and 4* is/are allowed.

6)☒ Claim(s) *3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-11* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants' arguments, filed November 06, 2003, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

2. Applicants' restatement of the response with traverse to the Restriction Requirement mailed January 21, 2003 is acknowledged. It is re-iterated that applicant did not distinctly and specifically point out the supposed errors in the restriction requirement; the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. The requirement is still deemed proper and is therefore made FINAL.

4. The new title has been accepted.

5. Claims 1-4 are examined on the merits.

Priority

6. The certified copies of foreign priority documents United Kingdom 0017376.5 and 0022943.5 have been received; therefore, the priority benefit to said document has been granted.

Claim Rejections - 35 USC § 112, Second Paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. This rejection is maintained with respect to claim 3, as recited in the previous office action mailed May 07, 2003.

10. Specific to line 2, the phrase "(-numerically less-)" causes the claim to be vague and indefinite because it is unclear what Applicants' intended meaning is for "(-numerically less-) as directed to the 30S ribosomal subunit. Clarification of the metes and bounds is required.

NEW MATTER UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

11. Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

12. This rejection is necessitated by Applicants amendments.

13. The limitation of "a crystal of a 30S ribosomal subunit having a resolution (-numerically less-) than about 3A" has not been found in the instant specification.

LACK OF ENABLEMENT UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claim 3 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a crystal structure of the Thermus thermophilus 30 S subunit having a resolution of 3.05 A, which have atom coordinates instantly disclosed, does not reasonably provide enablement for any 30 S subunit or any 30 S subunit having a resolution numerically less than about 3 A. Therefore, the specification is not enabled for those crystals beyond those, which consist of a structure as defined by the co-ordinates of table 1 having a resolution of 3.05 A. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

16. This rejection is maintained with respect to claim 3, as recited in the previous office action mailed May 07, 2003.

RESPONSE TO ARGUMENT

17. Specific to Applicant's argument via citing the instant specification, one of skill in the art would be enable to practice the claimed invention commensurate in scope with claim 3 due to the high degree of conservation of the ribosome structure being known as of the filing date of the application. Applicant's argument as directed to claim 3 has been fully considered and found to be unpersuasive as discussed below.

18. It is noted the pointed to disclosure supports that at the time of the instant invention it is known in the art that there is high degree of conservation of ribosome structure between prokaryotes of different species. However, the disclosure of high degree of conservation of ribosome structure between prokaryotes does not help Applicant overcome the fact that the instant specification disclose a 30 S subunit having a resolution of 3.05 A, but not one that is

numerically less than about 3 A. It is noted that structure conservation is only one of many characteristics of organisms such as prokaryotes, which have been used for the classification of said organisms. It is well known in the art that other characteristics (not a comprehensive example) such as gram stain, growth conditions, and metabolic properties have been widely used for classifying organisms of different species. Further, the knowledge of the structure of a protein is one of the many factors that contribute to the protein being able to be crystallized. Factors such as growth conditions and metabolic properties of an organism strongly determine the effort required to predictably crystallize a specific protein from said organism. It is these factors that determine the protein environment from which a protein is to be crystallized. The difference in the protein-surrounding environment due to the proteins being from organisms of different species greatly determines whether said proteins could be predictably crystallized using the same method.

19. Further, Applicant argues that the structural conservation is in the regions of structure essential for function (page 9, line 19) and the function being area responsible for the interaction of the 30 S protein with antibiotics (page 3, lines 6-20). It is noted that the area of the structural conservation of proteins is not the only area of said proteins that determines whether said protein could be predictably crystallized. Even with the regions of structure essential for function being conserved, the difference in the protein sequences, due to said sequences from different species, outside of the conserved regions greatly determines whether said proteins could be predictably crystallized using the same method.

20. Therefore, it is the characteristics of structural conservation and the above discussed factors that contribute to unpredictability of the art of protein crystallization as re-iterated

below. Therefore, the citation of the high degree of conservation of ribosome structure between prokaryotes of different species alone does enable one of skill in the art to predictably practice the claimed invention without undue experimentation.

21. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

22. It is acknowledged that the applicant has disclosed information to enable one skilled in the art to make the crystal of the Thermus thermophilus 30 S subunit having a resolution of 3.05 A (Page 16-18 and Table 1). However, it is well documented that protein crystallization is in essence a trial-and-error method, and the results are usually unpredictable (Drenth, J.). Further, as recently as November 1, 2002, Science published a New Focus article depicting the current state of the art for protein crystallization that supports the unpredictability of the art. In essences, protein crystallization is still a trial and error process because the current technology for producing protein for the crystallization process is unpredictable, which

results in high failure rate for proteins that are being crystallized. Therefore, researchers continue to have trouble generating sufficient protein required for the crystallization process (New Focus, Science, 2002). In light of the difficulty of the protein crystallization process, it is, therefore, unreasonable to expect one skilled in the art to any 30 S subunit crystal structure having a resolution numerically less than about 3 A, which consist of a structure as defined by the co-ordinates of table 1, without undue experimentation.

LACK OF WRITTEN DESCRIPTION 35 U.S.C. § 112, FIRST PARAGRAPH

23. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

24. Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

25. This rejection is maintained with respect to claim 3, as recited in the previous office action mailed May 07, 2003.

26. This rejection is necessitated by Applicants amendments.

RESPONSE TO ARGUMENT

27. Applicants argue by pointed to support that the instant specification provide adequate written description disclosure (page 4, lines 10-14) wherein an advantageous feature of the structure is that it defracts beyond 3A resolution. Applicants' argument has been fully considered and found to be unpersuasive due to the pointed to citation does not provide

adequate written description basis for the limitation of "30S ribosomal subunit having a resolution (-numerically less-) than about 3A."

28. It is re-iterated Applicants disclose the crystal structure of the *Thermus thermopilus* 30S subunit having a resolution of 3.05 A (Pages 16-18). However, Applicants do not provide disclosure for any 30S subunit having a resolution less than 3 A.

CONCLUSION

29. Claims 1, 2, and 4 are allowed.

30. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

31. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

32. This application contains claims 5-11 drawn to an invention nonelected with traverse in Previous Action, mailed May 07, 2003. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

33. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 193), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 872-9306.

34. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

35. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

36. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (571) 272-0549 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

C. Dune Ly
1/23/04

ARDIN H. MARSCHEL
PRIMARY EXAMINER